

Winter 2014 – 2015

# HELPING HANDS

FOR FRIENDS, FAMILY, AND SUPPORTERS OF THE CHILDREN'S GAUCHER RESEARCH FUND



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now takes years



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Prepare the road for FDA approval



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Gaucher community lost a friend,  
an advocate.



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Jay & Summer Warren...  
raise \$14,800



## 100% OF YOUR DONATION ... GOES TO RESEARCH

When we made the commitment to raise funds, fund medical research, and search for a cure, we made a promise to our donors. Our Promise; "100% of all donations will go directly to medical research". We have and we will continue to maintain that commitment. We are humbled with each donation, and amazed by your consistent support. We will continue to honor your generosity.

There is so much to say...

... and there is so little room in this newsletter to share all of the exciting things that are happening. The FDA/EMA Initiative to pave the road for approval of the first-ever drug therapy – the strengthening link between Gaucher disease and Parkinson's disease. But perhaps the most important event in 2014 is the important scientific discovery by Tony Futerman's laboratory in Israel – a discovery that was funded with your donations.

Gaucher Disease... History...  
from the beginning

Is there a disease? What causes it? Can we prevent, treat, or cure it? Answering these questions usually takes years of work, done by many investigators.

Today, progress with neuronopathic Gaucher disease is being made at an exponential rate. To demonstrate this point we have put together a Gaucher Disease Time-Line. Progress that used to be seen over decades, we are now seeing over a few short years. ■



DEBORAH MACRES  
AND GREG MACRES

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# GAUCHER DISEASE... HISTORY... FROM THE BEGINNING

## Adam & Eve to 1882 A.D.



**There was no Name!**  
– Children, adolescents, and adults would suffer and die from Gaucher disease. The disease had not yet been identified, categorized, or given a name.

## 1882 - Phillipe Charles Ernest Gaucher



**Is There A Disease?**  
– In 1882, French medical student Phillipe Charles Ernest Gaucher described a 32-year old woman whose spleen was enlarged. A postmortem exam revealed that cells in

the spleen were themselves enlarged. Gaucher described these clinical and pathological findings in his doctoral thesis. The enlarged cells (now called “Gaucher cells”) and spleen became signs of the disease, and Gaucher’s description of them enabled other physicians to diagnose people with Gaucher disease, and introduce the term into medical literature. In the ensuing years the list of identifiable symptoms grew.

Symptoms: enlarged spleen and liver - lung, kidney, and digestive problems - bone problems - growth retardation - joint pain - spontaneous bone fractures - nosebleeds, bruising and anemia - *in more severe cases usually involving children, the central nervous system (Brain) is also affected.*

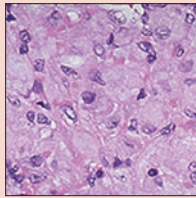
## 1884 - Johannes L. W. Thudichum



**Glycosphingolipids**  
– Johannes L. W. Thudichum, a pioneer in chemical biology, was the first to identify the presence of a novel class of lipids in the brain during his seminal studies in

London. Intrigued by their complex and multifaceted nature, Thudichum coined in 1884 the name ‘glycosphingolipids’, inspired by the ancient riddle of the Sphinx. It is now known that Glycosphingolipids play an important role in many neurologic disorders.

## 1934 - A. Aghion



*Enlarged cells in the spleen of a person with Gaucher Disease*

**What Causes Gaucher disease?** – French chemist A. Aghion discovers the chemical cause of the enlarged spleens and liver: a buildup of a lipid (fatty substance) called “glucocerebroside.”

This accumulation of lipid in the body is why Gaucher disease is now categorized in a group of diseases called “Storage Diseases”. This discovery led researchers to speculate why there was too much lipid - did people with Gaucher disease make too much of the lipid for their bodies to handle? Or did their bodies not break it down and dispose of it?

## 1964 - Roscoe Brady



**Gaucher Patients lack an Enzyme** – The answer to this question came during the early 1960s, when Dr. Roscoe Brady’s group at the National Institutes of Health showed that people with Gaucher disease made the lipid

normally but they did not make enough of the enzyme “glucocerebrosidase” to break it down and clear it out of the body. Later Dr. Brady’s group developed a convenient diagnostic test for Gaucher disease which works by measuring the activity of the enzyme glucocerebrosidase in white blood cells.

## 1966 - Roscoe Brady



**Can We Prevent, Treat, or Cure It?** – For Gaucher disease, physicians initially attempted to address the symptoms that accompany the disease.

They removed enlarged spleens, and performed liver transplants, blood transfusions, and orthopedic procedures.

In 1966, Dr. Roscoe Brady suggested a therapy for Gaucher disease based on replacing the enzyme. Using human placentas, Dr. Peter Pentchev of Dr. Brady’s team isolated a tiny sample of purified glucocerebrosidase (the enzyme). In 1973, two patients received this enzyme; because of the good biochemical results, Brady decided to develop a procedure to obtain larger quantities of the

enzyme for further clinical trials. Dr. Brady and his team at the National Institutes of Health continued their quest for enzyme replacement therapy for the next 20 years.

## 1984 - Edward Ginns



**Bone Marrow Transplantation (BMT)** – Dr. Edward Ginns at the National Institute of Health published a paper showing that a successful bone marrow transplant cures the systemic, but not the neurologic symptoms of Gaucher disease.

For Type 1 patients without brain involvement a bone marrow transplant becomes an optional treatment. Unfortunately this does not become standard treatment due to the significant side-effects and often life-threatening risks of a BMT.

## 1987 - Shoji Tsuji



**Why do some people make too little enzyme?** – The answer to this question came in 1987, when the first gene mutation that causes Gaucher disease was

discovered by Dr. Shoji Tsuji and coworkers at the University of Tokyo. Gaucher disease turned out to be an “autosomal recessive” genetic disease. This means that both of the glucocerebrosidase genes a person inherits - one from the mother and one from the father -- must be mutated for the person to have the disease.

## 1991 - Federal Drug Administration



**FDA Approval of Enzyme Replacement Therapy?** – On April 5, 1991, Dr. Brady’s

dream of enzyme replacement therapy (infusion of the missing glucocerebrosidase enzyme) was approved as a specific treatment for Gaucher disease by the Federal Drug Administration. Enzyme replacement therapy became an effective treatment for most people with Type 1 Gaucher disease (the form of Gaucher disease that does not affect the brain).

The question now; will enzyme replacement therapy be effective with neuronopathic Gaucher disease that affects the brain (Gaucher Type 2 & 3), and predominately affects young children.

## 1997 - Raphael Schiffmann



**Enzyme Replacement works for Type 1 Gaucher ... but ... Does Not Help the Brain?** – Patients with Neuronopathic Gaucher disease suffer

from various neurological problems and in most cases experience progressive brain disease that eventually leads to death. Dr. Raphael Schiffmann at the National Institutes of Health was tasked with determining if enzyme replacement would help with brain disease. After years of clinical research and accumulating vast amounts of data on children with neuronopathic Gaucher disease, Dr. Schiffmann determined that enzyme replacement therapy was not effective in preventing or curtailing brain disease progression.

## 2001 - Tony Futerman



**A Glycosphingolipids expert tackles neuronopathic Gaucher disease –** The Children's Gaucher Research Fund (CGRF) began funding

Dr. Tony Futerman at the Weizmann Institute of Science in 2001 in an effort to support basic

laboratory research – an effort to answer the basic molecular questions as to how the brain is affected by Gaucher disease. Over the following 13 years Futerman's team published 15 scientific articles – slowly piecing together the puzzle of brain disease.

## 2009 - Ellen Sidransky



**Gaucher disease linked to Parkinson's**

- Dr. Ellen Sidransky of the National Human Genome Research Institute had been intrigued by an observed link between Gaucher and Parkinson's for years. To explore it, she organized a consortium of 64 researchers at 16 institutions worldwide—virtually every Gaucher researcher in the world. They studied two common GBA variants in 5,691 people with Parkinson's disease, including 780 Ashkenazi Jews, and compared them to 4,898 disease-free individuals, including 387 Ashkenazi Jews. The Gaucher GBA Gene link to Parkinson's is now accepted by the research community. Research on one disease may shed light, or lead to treatment, for the other.

## 2014 - Tony Futerman



**Important Discovery - RIP3 Protein a culprit in Gaucher Brain Disease?**

– Dr. Tony Futerman's laboratory discovers a potential cause of neuronal death in neuronopathic Gaucher disease. If the RIP3 protein becomes

toxic and impairs brain neurons – why not simply inhibit this protein? Dr. Futerman did just this and the life span of his experimental mice increased from 40 to 180 days.

## 2015 - CGRF Increases funding of Futerman Lab



**Children's Gaucher Research Fund doubles annual funding** – The Board of Directors for the CGRF is encouraged

by the scientific progress and has awarded the Futerman Laboratory at the Weizmann Institute of Science with a \$400,000 research grant. ■

# FDA/EMA INITIATIVE

By Raphael Schiffmann M.D., M.H.Sc.

The overall goal of the CGRF is to help find effective therapy for neuronopathic Gaucher disease (Gaucher type 2 and type 3). In order to accomplish this, within our **FDA/EMA Initiative** we are focusing on two goals.

### Goal #1

First, an important part of the effort is to develop clinical tools (tests) to evaluate the degree of clinical abnormalities in patients. These may be used to assess the effect of novel therapies that are being developed. The clinical tool we need to develop should reflect the point of view of the patients and families and is often referred to as 'patient reported outcomes' or PRO. Towards that end, we wrote an initial open-ended questionnaire that we hope to administer in the coming months to patients and their family members, particularly in a patient/family meeting for neuronopathic Gaucher disease that we are planning. We shall use the responses obtained to construct another questionnaire with more specific questions. This questionnaire will be progressively refined and validated. Subsequently, we hope to progressively improve and then validate this new tool by comparing it with other ways to evaluate neuronopathic Gaucher patients.

.....  
"Today, we see potential therapies on the horizon and the CGRF is working hard to pave the road for drug approval...."  
.....

### Goal #2

The second goal we have is to improve our knowledge of the different forms of neuronopathic Gaucher disease. Since it is a rare disease, even doctors who specialize in this form of Gaucher disease have seen relatively few patients. For that, I recently visited, together with Dr. Marc C. Patterson, Chair, Division of Child and Adolescent Neurology, Mayo Clinic, Rochester, Minnesota, two major European medical centers. The centers were at the Center for Children and Adolescents at the Medical University of Mainz, Germany (with Dr. Eugen Mengel) and the Neuropediatric Unit of Armand-Trousseau Hospital in Paris, France (with Professor Thierry Billette de Villemeur and Dr. Nadia Belmatoug).

The physician experts in neuronopathic Gaucher disease at their respective centers were extremely kind to allow us to see most of their Gaucher type 3 patients. We spent 3-6 days in each medical center. In total, we encountered 28 children and adult patients (age range 2-41 years). This experience taught us that the clinical presentation and natural course of Gaucher type 3 is extremely variable. No two patients are alike. The clinical variability is in part due to different genetic mutations of the Gaucher gene but also to the different ethnic background of patients. In addition to Europeans, we saw patients who were of Turkish, African, Lebanese, Palestinian and Thai ancestry. We think that seeing these international patients will help us to better understand the disease, design improved clinical trials, and cement the transnational co-operation necessary for such studies.

### Why Now?

When the CGRF began some 15 years ago this initiative was not on our radar. There was little research on neuronopathic Gaucher disease much less the hope that a therapy was on the horizon. Today, we see potential therapies on the horizon and the CGRF is working hard to pave the road for drug approval, thus expediting the delivery of these therapies to the children who so desperately need them. ■

**RAPHAEL SCHIFFMANN M.D., M.H.SC.**  
**Baylor Research Institute**  
**Chairman – CGRF Scientific Advisory Board**



# In Memory Of Betty Seely

Betty with her grandson Gregory Austin Macres. Gregory passed away from Gaucher disease in 1997, at the age of 4.



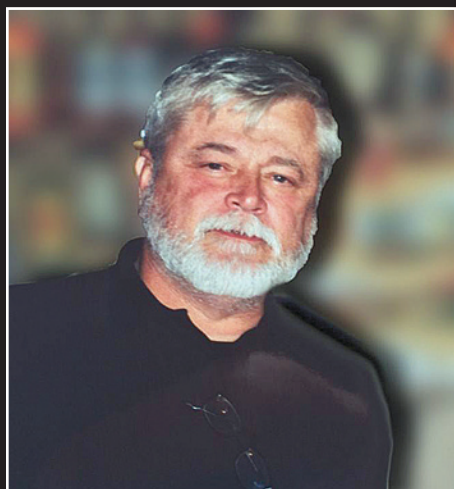
**Betty Seely**, mother of Deborah Macres (Founder of the CGRF) passed away on August 17, 2014.

Betty's love and devotion to her family will be deeply missed. We know she is in Heaven holding and loving her grandson, Gregory Austin.

The Macres family would like to thank the many family and friends who made a donation to the CGRF in Betty's honor, and in her memory. Your thoughtfulness would make her proud. ■

## In Grateful Memory of John A. Barranger, M.D., Ph.D.

### **A CHAMPION FOR THOSE WITH LYSOSOMAL STORAGE DISORDERS**



On May 25, 2014, the Gaucher community and the Lysosomal disease community at large lost a friend, an advocate, and a great mind. He was a man who devoted himself to research and to patient care; always an advocate for those who suffer from Lysosomal storage disorders. We were honored that Dr. Barranger served on the Scientific Advisory Board for the Children's Gaucher Research Fund.

Dr. Barranger earned his Ph.D. and M.D. at the University of Southern California and completed his pediatric residency at the University of Minnesota in 1976. He held positions at Children's Hospital Los Angeles, the University of Pittsburgh Medical Center and was Professor of Human Genetics, Molecular Genetics and Biochemistry and Pediatrics at the University of Pittsburgh.

Dr. Barranger was a pioneer in the field of enzyme replacement therapy; during his Fellowship at the National Institutes of Health (NIH) he was instrumental in developing the first successful treatment for Gaucher Disease. Most recently, he founded the Lysosomal Storage Disease Clinical Care Network (LSDCCN) to establish treatment centers across the United States. Dr. Barranger dedicated his career to improving the quality of life for patients with lysosomal diseases; his efforts reached thousands.

He will be missed. ■

"Finding a doctor experienced in the lysosomal storage disorders is often a challenge for patients. A doctor to guide care and provide a place to receive infusions is what everyone deserves. That access is critical to the best outcomes in the LSDs." ...

**John A. Barranger, M.D., Ph.D.**



# CHASEN'TAILZ FUNDRAISER



## In Honor of Chase Edward Warren



1<sup>st</sup> Annual ChaseN'Tailz KDW Fishing Tournament in memory of our 10 month old son Chase Warren who passed away last year from Gaucher Type 2. We are deep rooted into the boating community and rallied our friends and business's for a great cause and to keep Chase's legacy alive. We had 31 boats enter even though the weather wasn't great everyone pushed on! After a day of fishing and an evening of Music, Food, Raffles & a Silent Auction we proudly will be donating \$14,800.00 for Gaucher 2/3 research in Chase's memory. We are proud to be Chase's parents and are certain he is continuing to impact and educate others on rare fatal childhood diseases.

**\$14,800 Raised for  
Medical Research**

*kindest Regards,  
Jay & Summer Warren  
Parents to an Angel  
[www.ChaseNtailz.com](http://www.ChaseNtailz.com)*

Progress made by the Children's Gaucher Research Fund would not be possible without our generous donors, and without the commitment of families who have lost a child to neuronopathic Gaucher disease. Many families choose to honor their child's life by fundraising and supporting our research effort – Summer and Jay Warren have made this commitment.



"After a day of singing and cuddles he passed away in his crib surrounded by love and family on August 7, 2013. A piece of our hearts died with Chase that day and we vowed to help others. Two days after Chase passed we received the fatal diagnosis of Gaucher Type 2; there is not a treatment or a cure. These children and parents have no options as with most neurological childhood disease. This is why we are proud to have started ChaseN'Tailz Fishing Tournament in Memory of our beautiful son. We hope to spread awareness about rare diseases and raise funds for them. Most of these diseases are closely related and research for one greatly impacts 16 others. Please help us on our journey to find a treatment."

## CGRF MILESTONES

### 1993

- ◆ Founders son Gregory born
- ◆ Gregory diagnosed with nGD

### 1997

- ◆ Gregory passes away
- ◆ Memorial fund established

### 1997-1999

- ◆ Surprising growth of memorial fund

### 1999

- ◆ Children's Gaucher Research Fund established as 501(c)(3) nonprofit
- ◆ Encouragement received from Research Community

### 1999-Present

- ◆ Families affected by nGD join the fight
- ◆ Attracted thousands of people to our network
- ◆ Funded eight important nGD research Projects
- ◆ Funded creation of an Inducible Gaucher Mouse
- ◆ Hosted five international medical conferences

### 2012

- ◆ Conference of world experts: Pathological Mechanism in Neuronal forms of Gaucher Disease - Recent Discoveries – Future Direction
- ◆ Evaluation of the Inducible nGD Mouse Model
- ◆ FDA/EMA Initiative for drug approval

### 2014

- ◆ Over **\$2.3 Million** raised
- ◆ Continued funding of scientific research
- ◆ Resulting in 15 scientific publications
- ◆ Major scientific discovery





## ONLINE DONATIONS

can be made by visiting  
[www.childrensgaucher.org](http://www.childrensgaucher.org)

OR

[www.cgrf.org](http://www.cgrf.org)

All family stories can be read on the web site.

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3. We *do not* hire professional fundraising companies who keep 50% of donated funds.
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5. All administrative costs are paid for by the *founders*.

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 All family stories can be  
 read on the website.

Contributions Payable To:  
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## Children's Gaucher Research Fund



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